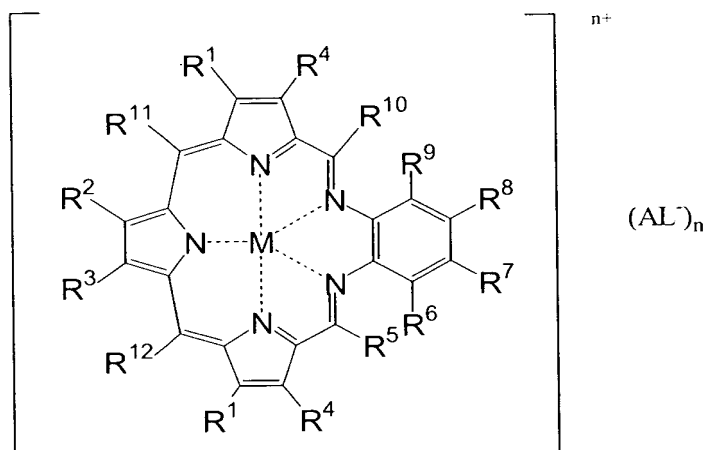


WHAT IS CLAIMED IS:

1. A compound of the Formula:



Formula I

5 wherein:

M is a monovalent, divalent, trivalent, or tetravalent metal cation;

AL is an apical ligand derived from a group consisting of gluconic acid, phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid;

10 n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;

$R^1, R^2, R^3, R^4, R^6, R^7, R^8,$  and  $R^9$ , are independently chosen from the group consisting of hydrogen, halogen, hydroxyl, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted haloalkyl; alkylalkoxy, nitro, acyl, optionally substituted alkoxy, saccharide, optionally substituted amino, carboxyl, optionally substituted carboxyalkyl, optionally substituted carboxamide, optionally substituted carboxamidealkyl, optionally substituted heterocycle, optionally substituted cycloalkyl, optionally substituted arylalkyl, optionally substituted heteroarylalkyl, optionally substituted heterocycloalkylalkyl; and a

20 group  $-X-Y$ , in which X is a covalent bond or a linker and Y is a catalytic group, a chemotherapeutic agent, or a site-directing molecule, and;

R<sup>5</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> are independently hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted alkoxy, optionally substituted carboxyalkyl, or optionally substituted carboxyamidealkyl; with the proviso that the halogen is other than iodide and the haloalkyl is other than iodoalkyl.

2. The compound of Claim 1, wherein M is a divalent metal cation chosen from Ca(II), Mn(II), Co(II), Cd(II) and Fe(II), or a trivalent metal cation chosen from Mn(III), Co(III), Fe(III), Y(III), In(III), Sm(III), Eu(III), Gd(III), Tb (III), Dy(III) and Lu(III).

3. The compound of Claim 2, wherein the apical ligand is selected from pyruvate, phosphate, glucuronate, carbonate, sulfonate, oxalate and lactate.

4. The compound of Claim 3, wherein:  
R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are optionally substituted alkyl of 1-10 carbon atoms, R<sup>5</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are hydrogen or alkyl of 1-6 carbon atoms; and  
R<sup>7</sup> and R<sup>8</sup> are optionally substituted alkoxy or alkylalkoxy.

5. The compound of Claim 4, wherein R<sup>1</sup> at each occurrence is hydroxyalkyl, R<sup>4</sup> at each occurrence is alkyl, and R<sup>5</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are hydrogen.

6. The compound of Claim 5, wherein R<sup>1</sup> at each occurrence is 2-hydroxyethyl or 3-hydroxypropyl, R<sup>4</sup> at each occurrence is methyl or ethyl, and R<sup>7</sup> and R<sup>8</sup> are both  
-O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>x</sub>CH<sub>3</sub>, where x is an integer of 2-5.

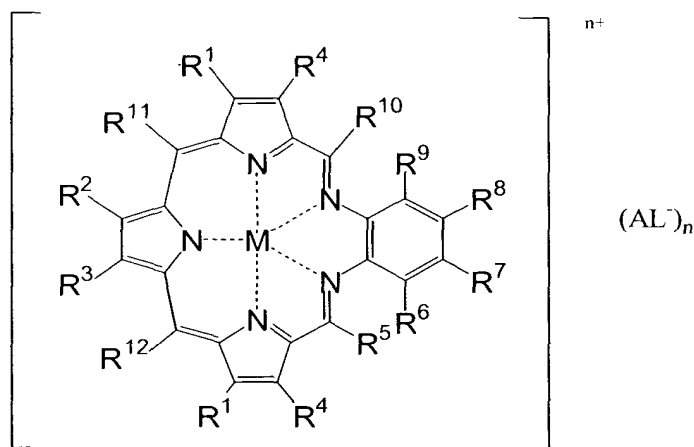
7. The compound of Claim 6, wherein x is 3.

8. The compound of Claim 7, wherein M is Lu(III), Mu(II), Mu(III) or Gd(III) and AL is derived from glucuronic acid, phosphoric acid, pyruvic acid, methane sulfonic acid, and oxalic acid.

5 9. The compound of Claim 8, wherein R<sup>1</sup> is 3-hydroxypropyl, R<sup>2</sup> and R<sup>3</sup> are ethyl, R<sup>4</sup> is methyl, and R<sup>7</sup> and R<sup>8</sup> are 2-[2-[(2-methoxyethoxy)ethoxy]ethoxy].

10. The compound of Claim 9, wherein M is Lu(III) and the apical ligand is derived from gluconic acid, namely the lutetium (III) complex of: 4,5-diethyl-  
10,23-dimethyl-9,24-bis(3-hydroxy propyl)-16,17-bis[2-[2-(2  
methoxyethoxy)ethoxy]ethoxy]pentaazapentacyclo-  
[20.2.1.1<sup>3,6</sup>.1<sup>8,11</sup>.0<sup>14,19</sup>]heptacos-1,3,5,7,9,11(27),12,14,16,18,20,22(25),23-  
tridecaene bis gluconate.

11. A compound of Formula I



Formula I

wherein:

M is selected from Gd(III), Mn(II), Mn(III) and Lu(III);

AL is an apical ligand derived from a group consisting of gluconic acid,  
phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic  
acid;

n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;

R<sup>1</sup> represents -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH;

R<sup>2</sup> and R<sup>3</sup> represent -CH<sub>2</sub>CH<sub>3</sub>;

R<sup>4</sup> represents -CH<sub>3</sub>;

5 R<sup>5</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> represent H; and

R<sup>7</sup> and R<sup>8</sup> represent -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>3</sub>CH<sub>3</sub>.

10 12. A method for treating a disease or condition in a mammal resulting from the presence of neoplastic tissue, neovascularization, or an atheroma, which method comprises:

- a) administering to a mammal in need of such treatment a therapeutically effective amount of a compound of claim 1, and
- b) treating the area in proximity to the neoplastic tissue with a therapeutic energy means or with a chemotherapeutic agent; or
- 15 c) treating the area in proximity to the neovascularization or atheroma with a therapeutic energy means.

20 13. The method of Claim 12, wherein the therapeutic energy means is chosen from photoirradiation, ionizing radiation, neutron irradiation, and ultrasound.

14. The method of Claim 13, wherein M is a divalent metal cation chosen from Ca(II), Mn(II), Cd(II) and Fe(II), or a trivalent metal cation chosen from Mn(III), Co(III), Y(III), In(III), Eu(III), Gd(III), and Lu(III).

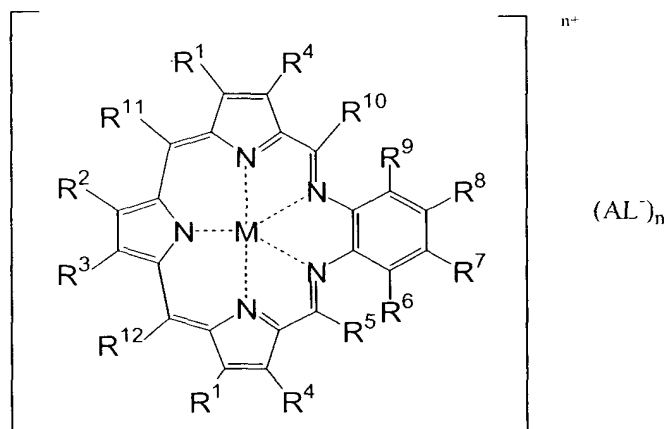
25 15. The method of Claim 14, wherein the apical ligand is derived from the group consisting of gluconic acid, phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid.

30 16. The method of Claim 15, wherein:  
R<sup>1</sup> R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are optionally substituted alkyl of 1-10 carbon atoms,

$R^5$ ,  $R^6$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are hydrogen or alkyl of 1-6 carbon atoms;  
and

$R^7$  and  $R^8$  are optionally substituted alkoxy or alkylalkoxy.

- 5      17.    The method of Claim 16, wherein  $R^1$  at each occurrence is -  
CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH,  $R^4$  at each occurrence is -CH<sub>3</sub>,  $R^7$  and  $R^8$  are -  
O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>x</sub>CH<sub>3</sub>, wherein x represents an integer of 1-5, and  $R^5$ ,  $R^6$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$   
and  $R^{12}$  are hydrogen.
- 10     18.    The method of Claim 17 wherein x is 3.
- 15     19.    The method of Claim 18, wherein M is Lu(III) or Gd(III) and AL is  
derived from glucuronic acid, phosphoric acid, pyruvic acid, methane sulfonic  
acid, and oxalic acid.
- 20     20.    The method of Claim 19 wherein M is Lu(III) and the apical ligand is  
derived from gluconic acid, namely the lutetium (III) complex of: 4,5-diethyl-  
10,23-dimethyl-9,24-bis(3-hydroxy propyl)-16,17-bis[2-[2-(2  
methoxyethoxy)ethoxy]ethoxy]pentaazapentacyclo-  
[20.2.1.1<sup>3,6</sup>.1<sup>8,11</sup>.0<sup>14,19</sup>]heptacos-1,3,5,7,9,11(27),12,14,16,18,20,22(25),23-  
tridecaene bis gluconate.
- 25     21.    A method for treating a disease or condition in a mammal resulting from  
the presence of neoplastic tissue, neovascularization, or an atheroma, which  
method comprises:
- (a)    administering to a mammal in need of such treatment a  
therapeutically effective amount of a compound of Formula I



Formula I

wherein:

5 M is selected from Gd(III), Mn(II), Mn(III) and Lu(III);

AL is an apical ligand derived from a group consisting of gluconic acid, phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid;

n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;

10 R<sup>1</sup> represents -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH;

R<sup>2</sup> and R<sup>3</sup> represent -CH<sub>2</sub>CH<sub>3</sub>;

R<sup>4</sup> represents -CH<sub>3</sub>;

R<sup>5</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> represent H; and

R<sup>7</sup> and R<sup>8</sup> represent -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>3</sub>CH<sub>3</sub>; and

15

- (b) treating the area in proximity to the neoplastic tissue with a therapeutic energy means or with a chemotherapeutic agent; or
- (c) treating the area in proximity to the neovascularization or atheroma with a therapeutic energy means.

20

22. A pharmaceutical composition comprising at least one pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 1.

23. The composition of Claim 22, wherein the apical ligand is derived from the group consisting of gluconic acid, phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid.

24. The composition of Claim 23, wherein:

$R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are optionally substituted alkyl of 1-10 carbon atoms;  
 $R^5$ ,  $R^6$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are hydrogen or alkyl of 1-6 carbon atoms;

and

$R^7$  and  $R^8$  are optionally substituted alkoxy or alkylalkoxy.

25. The composition of Claim 24, wherein  $R^1$  at each occurrence is 2-hydroxyethyl or 3-hydroxypropyl;

$R^4$  at each occurrence is methyl or ethyl;

$R^5$ ,  $R^6$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are hydrogen; and

$R^7$  and  $R^8$  are both  $-O(CH_2CH_2O)_xZ$ , where x is an integer of 2-5, and Z is

hydroxy or alkyl of 1-6 carbon atoms.

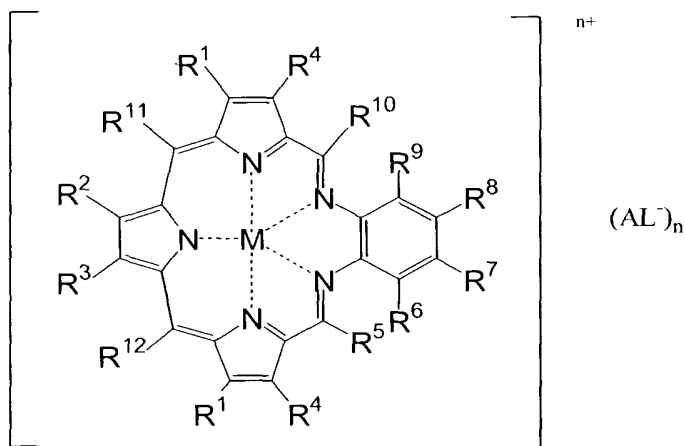
26. The composition of Claim 25, wherein Z is methyl or hydroxy and x is 1-3.

27. The composition of Claim 26, wherein M is Lu(III) or Gd(III) and the apical ligand (AL) is selected from pyruvate, phosphate, glucuronate, carbonate, sulfonate, oxalate and lactate.

28. The composition of Claim 27, wherein  $R^1$  is 3-hydroxypropyl,  $R^2$  and  $R^3$  are ethyl,  $R^4$  is methyl, and  $R^7$  and  $R^8$  are 2-[2-[(2-methoxyethoxy)ethoxy]ethoxy].

29. The composition of Claim 28, wherein M is Lu(III) and the apical ligand is derived from gluconic acid, namely the lutetium (III) complex of: 4,5-diethyl-10,23-dimethyl-9,24-bis(3-hydroxy propyl)-16,17-bis[2-[2-(2-methoxyethoxy)ethoxy]ethoxy]pentaazapentacyclo-  
 5 [20.2.1.1<sup>3,6</sup>.1<sup>8,11</sup>.0<sup>14,19</sup>]heptacos-1,3,5,7,9,11(27),12,14,16,18,20,22(25),23-tridecaene bis gluconate.

30. A pharmaceutical composition comprising at least one pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of  
 10 Formula I



Formula I

wherein:

M is selected from Gd(III), Mn(II), Mn(III) and Lu(III);

AL is an apical ligand derived from a group consisting of gluconic acid, phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid;

n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;

R<sup>1</sup> represents -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH;

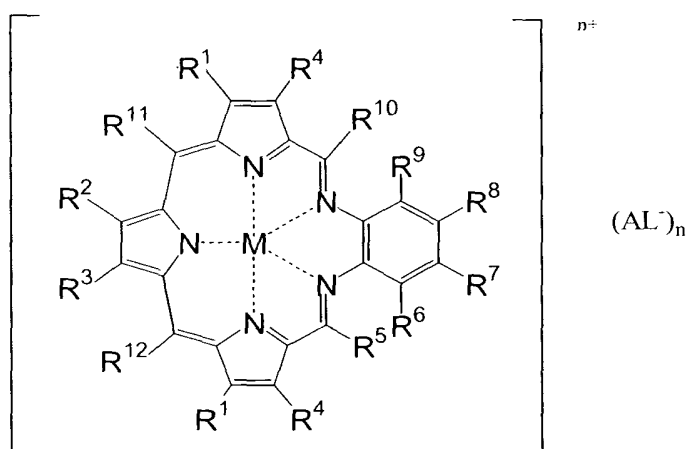
R<sup>2</sup> and R<sup>3</sup> represent -CH<sub>2</sub>CH<sub>3</sub>;

R<sup>4</sup> represents -CH<sub>3</sub>;



$R^5, R^6, R^9, R^{10}, R^{11}$ , and  $R^{12}$  represent H; and  
 $R^7$  and  $R^8$  represent  $-O(CH_2CH_2O)_3CH_3$ .

31. A pharmaceutical composition comprising at least one pharmaceutically  
 5 acceptable excipient and a therapeutically effective amount of a compound of  
 Formula I

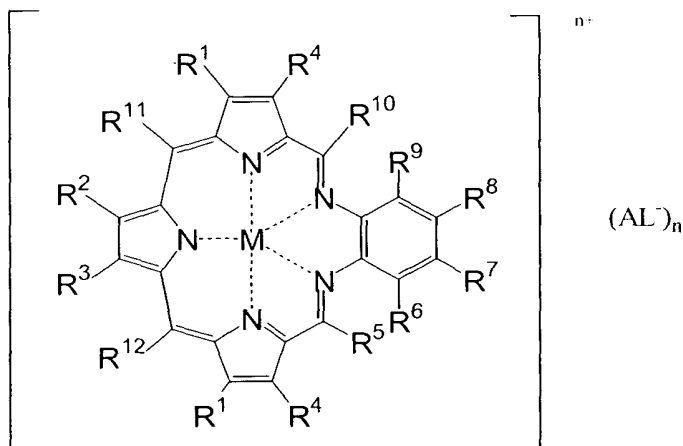


Formula I

wherein:

- 10 M represents Gd(III);  
 AL is an apical ligand derived from a group consisting of gluconic acid,  
 phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic  
 acid;  
 n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;  
 15  $R^1$  represents  $-CH_2CH_2CH_2OH$ ;  
 $R^2$  and  $R^3$  represent  $-CH_2CH_3$ ;  
 $R^4$  represents  $-CH_3$ ;  
 $R^5, R^6, R^9, R^{10}, R^{11}$ , and  $R^{12}$  represent H; and  
 $R^7$  and  $R^8$  represent  $-O(CH_2CH_2O)_3CH_3$ .

32. A pharmaceutical composition comprising at least one pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of Formula I



5

Formula I

wherein:

M represents Lu(III);

AL is an apical ligand derived from a group consisting of gluconic acid, phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid;

10

n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;

R<sup>1</sup> represents -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH;

R<sup>2</sup> and R<sup>3</sup> represent -CH<sub>2</sub>CH<sub>3</sub>;

R<sup>4</sup> represents -CH<sub>3</sub>;

15

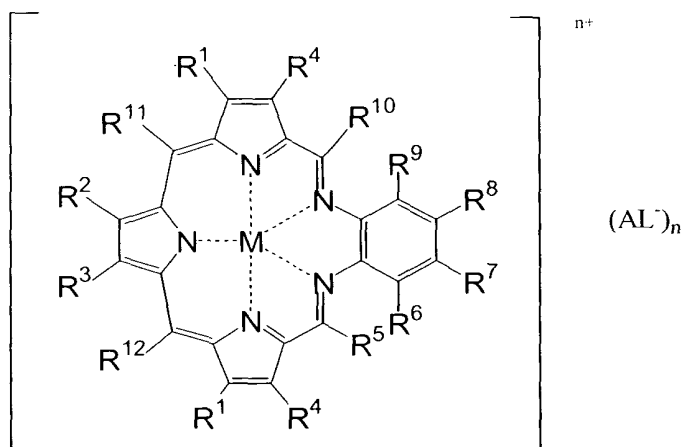
R<sup>5</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> represent H; and

R<sup>7</sup> and R<sup>8</sup> represent -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>3</sub>CH<sub>3</sub>.

33. A method for treating a disease or condition in a mammal resulting from the presence of neoplastic tissue, neovascularization, or an atheroma, which method comprises:

20

- (a) administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Formula I



wherein:

5 M represents Gd(III);

AL is an apical ligand derived from a group consisting of gluconic acid, phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid;

n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;

10 R<sup>1</sup> represents -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH;

R<sup>2</sup> and R<sup>3</sup> represent -CH<sub>2</sub>CH<sub>3</sub>;

R<sup>4</sup> represents -CH<sub>3</sub>;

R<sup>5</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> represent H; and

R<sup>7</sup> and R<sup>8</sup> represent -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>3</sub>CH<sub>3</sub>; and

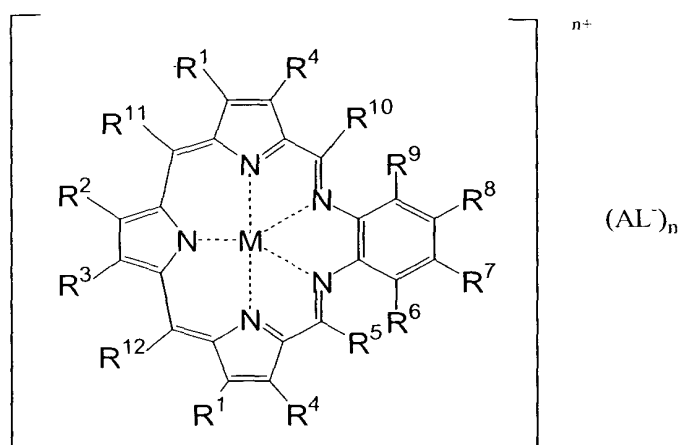
15

- (b) treating the area in proximity to the neoplastic tissue with a therapeutic energy means or with a chemotherapeutic agent; or
- (c) treating the area in proximity to the neovascularization or atheroma with a therapeutic energy means.

20

34. A method for treating a disease or condition in a mammal resulting from the presence of neoplastic tissue, neovascularization, or an atheroma, which method comprises:

- 5 (a) administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Formula I



wherein:

M represents Lu(III);

10 AL is an apical ligand derived from a group consisting of gluconic acid, phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid;

n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;

R<sup>1</sup> represents -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH;

15 R<sup>2</sup> and R<sup>3</sup> represent -CH<sub>2</sub>CH<sub>3</sub>;

R<sup>4</sup> represents -CH<sub>3</sub>;

R<sup>5</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> represent H; and

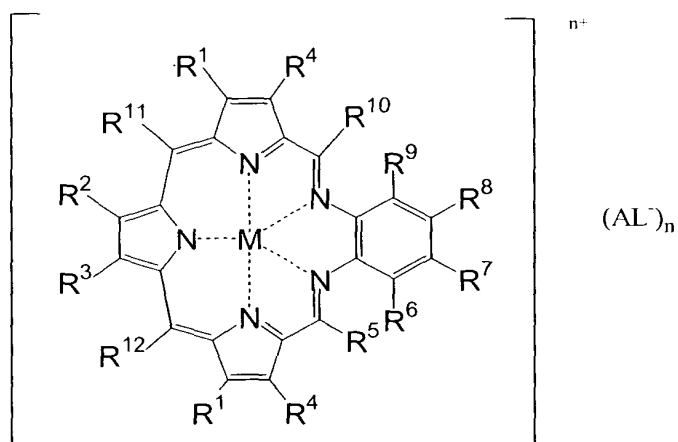
R<sup>7</sup> and R<sup>8</sup> represent -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>3</sub>CH<sub>3</sub>; and

- 20 (b) treating the area in proximity to the neoplastic tissue with a therapeutic energy means or with a chemotherapeutic agent; or

- (c) treating the area in proximity to the neovascularization or atheroma with a therapeutic energy means.

35. A compound of Formula I

5



Formula I

wherein:

M represents Gd(III);

AL is an apical ligand derived from a group consisting of gluconic acid,  
10 phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid;

n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;

R<sup>1</sup> represents -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH;

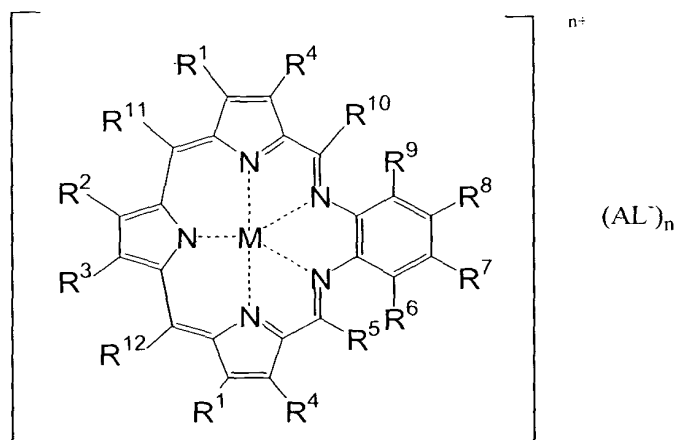
R<sup>2</sup> and R<sup>3</sup> represent -CH<sub>2</sub>CH<sub>3</sub>;

15 R<sup>4</sup> represents -CH<sub>3</sub>;

R<sup>5</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> represent H; and

R<sup>7</sup> and R<sup>8</sup> represent -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>3</sub>CH<sub>3</sub>.

36. A compound of Formula I



Formula I

wherein:

M represents Lu(III);

5 AL is an apical ligand derived from a group consisting of gluconic acid, phosphoric acid, glucuronic acid, lactic acid, pyruvic acid, and p-toluene sulfonic acid;

n is 1 when M is a divalent cation, or n is 2 when M is a trivalent cation;

R<sup>1</sup> represents -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH;

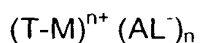
10 R<sup>2</sup> and R<sup>3</sup> represent -CH<sub>2</sub>CH<sub>3</sub>;

R<sup>4</sup> represents -CH<sub>3</sub>;

R<sup>5</sup>, R<sup>6</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> represent H; and

R<sup>7</sup> and R<sup>8</sup> represent -O(CH<sub>2</sub>CH<sub>2</sub>O)<sub>3</sub>CH<sub>3</sub>.

15 37. A process for preparing a metallotexaphyrin having the formula:



wherein:

T is a texaphyrin;

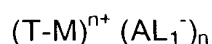
20 M is a divalent or trivalent metal cation constrained within the binding cavity of the texaphyrin;

AL is an apical ligand; and

n is an integer of 1-5;

comprising:

- 5 (a) contacting an apical ligand (AL)H with a quarternary amine resin;  
(b) contacting the resin complex produced in step a) with a  
metallotexaphyrin of the formula:



10 in which T and M are as defined above;

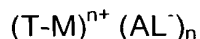
(AL<sub>1</sub>) represents a displaceable apical ligand; and

n is an integer of 1-5.

15 38. The process of Claim 37, wherein M is Lu(III) or Gd(III), (AL<sub>1</sub>) is acetate,  
and n is 2.

39. The process of Claim 38, wherein (AL)H is chosen from formic acid,  
propionic acid, butyric acid, pentanoic acid, 3,6,9-trioxodecanoic acid, 3,6-  
dioxoheptanoic acid, 2,5-dioxoheptanoic acid, methylvaleric acid, glycolic acid,  
20 pyruvic acid, oxalic acid, malic acid, malonic acid, succinic acid, maleic acid,  
fumaric acid, tartaric acid, citric acid, methanesulfonic acid, ethanesulfonic acid,  
benzoic acid, salicylic acid, 3-fluorobenzoic acid, 4-aminobenzoic acid, cinnamic  
acid, mandelic acid, and p-toluene-sulfonic acid.

25 40. A process for preparing a metallotexaphyrin having the formula:



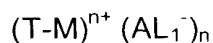
wherein:

T is a texaphyrin;

30 M is a divalent or trivalent metal cation constrained within the binding cavity of  
the texaphyrin;

AL is an apical ligand; and  
n is an integer of 1-5;  
comprising:  
contacting a metallotexaphyrin of the formula:

5



in which T and M are as defined above;  
(AL<sub>1</sub>) represents a displaceable apical ligand; and  
n is an integer of 1-5;  
with an excess of an apical ligand (AL)H;  
at a temperature of 20-100°C.

10

15

41. The process of Claim 40, wherein M is Lu(III) or Gd(III), (AL<sub>1</sub>) is acetate,  
and n is 2.

20

42. The process of Claim 40, wherein (AL)H is chosen from formic acid,  
propionic acid, butyric acid, pentanoic acid, 3,6,9-trioxodecanoic acid, 3,6-  
dioxoheptanoic acid, 2,5-dioxoheptanoic acid, methylvaleric acid, glycolic acid,  
pyruvic acid, oxalic acid, malic acid, malonic acid, succinic acid, maleic acid,  
fumaric acid, tartaric acid, citric acid, methanesulfonic acid, ethanesulfonic acid,  
benzoic acid, salicylic acid, 3-fluorobenzoic acid, 4-aminobenzoic acid, cinnamic  
acid, mandelic acid, and p-toluene-sulfonic acid.

25